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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/552,272	04/19/2000	Li Fang	1113CIP4PCTUS00	3198

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EXAMINER	
EPPS FORD, JANET L	
ART UNIT	**PAPER NUMBER**
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/552,272	FANG ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,6,10,14-19,23-28,32-37,50 and 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,5,6,10 and 14* is/are allowed.

6)☒ Claim(s) *16-19,23-28,32-37,50 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 5-6, 10, 14-19, 23-27, 28, 32-37, 50, and 53 are presently pending.

2. The previously indicated allowability of claims 16-19, 23-27, 28, 32-37, 50, and 53 is withdrawn in response to the following grounds of rejection.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 16-19, 23-27, 28, 32-37, 50, and 53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (Written description).

5. Claim 16, and those claims dependent therefrom recite:

"A nucleic acid vector that enhances translation of a gene transcript under conditions that elicit a cold-shock response in a bacterium, comprising a ***downstream box***,....."

Claim 18, further recites:

"A nucleic acid vector of Claim 16 further comprising a ***cold box***, wherein said vector enhances translation of a gene transcript and directs prolonged production of a protein encoded by the transcript under conditions that elicit a cold shock response in a bacterium."

Claim 19 recites:

"A nucleic acid vector that enhances the translation of a gene transcript....comprising..***a downstream box...***"

Claims 23-27, 32-33, and 35-37 depend from claim 16, 18 or 19.

Claim 28 recites: "A nucleic acid vector comprising...***a downstream box***...."

Claims 34 depend from claim 28.

Claim 50 recites: "A vector....comprising a ***downstream box***,...."

The specification as filed (page 4, 3rd paragraph) describes the "downsteam box" as a 14 base downstream box located 12 bases downstream of the translation initiation codon of the *cspA mRNA,* which is partially complementary to a region called anti-downstream box of 16S rRNA.."

Pages 19-20 of the specification as filed recites a *non-limiting* description of the structure of the downstream box as recited in the instant claims:

> Below are several non-limiting examples of suitable DBs for the mRNA construct. Each of the following DB is substantially complementary to the ADB of the *E. coli* 16S rRNA which ADB has the sequence:

ADB 3' (-1481) UACUUAGUGUUUCA (-1469) 5' (SEQ ID NO:1)

DB #1: 5' AUGACUGGUAUCGU 3' (SEQ ID NO:2)

DB #2: 5' AUGACUGGUUUCGU 3' (SEQ ID NO:3)

DB #3: 5' AUGACUGGUUUAGU 3' (SEQ ID NO:4)

DB #4: 5' AUGAGUUAUGUAGA 3' (SEQ ID NO:5)

DB #5: 5' AUGGCGAAAAGAAU 3' (SEQ ID NO:6)

A suitable mRNA construct according to the invention can be constructed using any one of the above DBs, or other suitable DB, for example:

5' AUG$X_{(n)}$AUGACUGGUAUCGU 3' (SEQ ID NO:7)

where n is a whole number from 0 to 30, and X is G, C, U, or A, wherein each occurrence of X may be the same as or different from any other occurrence of X. Alternatively, the 5' end of the DB overlaps the initiation codon.

The above description of the downstream box of the instant invention is clearly described as "substantially complementary" to the anti-downstream box of E. coli 16S ribosomal RNA. The specification does not provide a definition of the term "substantially" therefore the exact scope of the genus of downstream boxes encompassed by the instant claims is not adequately described. Moreover, the above passage recites that the above definition of the claimed downstream box encompassed by the instant invention is *non-limiting,* therefore again, it is unclear what other sequences may function as a downstream box. Therefore, again, the structure of the full scope of downstream boxes encompassed by the instant claims is not adequately defined.

Pages 23-24 of the specification as filed recites the following: "A similar effect is noted with respect to complementarity of the DB of the overexpressed mRNA and the

ADB of the bacterial 16S rRNA. Overexpression of an mRNA comprising a DB with 100% complementarity will be more efficient in binding to the ADB than will be an mRNA comprising a DB with lesser (75%) complementarity. Thus, the protein blocking effect of an mRNA having a more highly complementary DB will be more pronounced compared to that of an mRNA having a less complementary DB. *Therefore, when using an mRNA having a less complementary DB*, it may be useful to express the mRNA in a higher copy number to achieve the same or similar antibiotic results as with an mRNA having a more complementary DB."

The specification as filed defines the cold-box as a DNA sequence that is capable of prolonging the normally transient expression of the cold shock genes during the adaptation of a bacterium to physiological stress that elicits the cold shock response. According to the specification, in regards to *E. coli* cold-shock genes, the cold box is situated within the first 25 nucleotide of the 5'UTR of cold shock genes (see pages 25-26). The specification further describes the cold box of multiple *E. coli* cold shock genes (*cspA, cspB, cspG, and csdA)* as situated between nucleotides +1 and +11 of the 5' UTR. However, it is not clear that the sequences recited in the specification as filed as corresponding to a "cold box" is necessarily useful to predict the structures of cold boxes from all strains of bacteria.

To satisfy the written description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, ***935*** *F.3d* at 1563; see also Lockwood v. American Airlines, Inc., 107

F.3d 1565, 1572 (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In *re Gosteli,* 872 F. 2d 1008, 1012 (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood,* 107 F.3d 1572.

Furthermore, the courts held that an adequate description of a biomolecule .."'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." *Eli Lilly,* 119 F. 3d at 1566 (quoting *Fiers,* 984 F. 2d at 1171). Moreover, the court said that "[c]laiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement; it is an attempt to preempt the future before it has arrived." *Fiers,* 984 F. 2d at 1171.

Additionally, MPEP § 2163 recites: "[A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence."

Therefore, as stated above, since the specification as filed does not provide a clearly and unambiguous nucleotide structure of the downstream box or the cold box as recited in the instant claims, it is concluded that Applicants were not in possession of the full scope of the isolated nucleic acids encompassed by the instant claims.

6. Claims 1, 5-6, 10, 14-15 allowable over the prior art searched.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

8. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

9. Claims 16-19, 23-28, 32-37, 50, and 53 are rejected under 35 U.S.C. 102(a or e) as being anticipated by Inouye et al. (US Patent No. 5,714,575).

Inouye et al. discloses the sequence of SEQ ID NO: 5.

This sequence comprises nucleotides 1-11, 56-117 and 123-135 of SEQ ID NO: 55, and SEQ ID NO: 48 of the underlined sequences of SEQ ID NO: 5 represent the respective sequences:

SEQ ID NO: 5:

A**ACGGUUUGACG**UACAGACCAUUAAAGCAGUGUAGUAAGGCAAGUCCCUUCAAG AGU**UAUCGUUGAUACCCCUCGUAGUGCACAUUCCUUUAACGCUUCAAAAUCUG U AAAGCACGCC**-AUAUC**GCCGAAAGGCACA**CUUAAUUAUUAAAGGUAAUACACU. Absent evidence to the contrary, the various sequences set forth in this sequence comprise downstream and cold box sequences.

SEQ ID NO: 6 of Inouye et al. comprises the sequence of SEQ ID NO: 49, note the following underlined sequence in SEQ ID NO: 6.

SEQ ID NO: 6:

CGUCGGUUUGAAGAACAGACGAUAUACGAAGUAGUUUACUAAAGCAGUUCUCAU UUCAGGUGUUAUUCACUUAUUCCUUCUUUGAGUCUCUCCAAUUAAGUACGAAGU CGUUUCUGUUAUGCAAACCAUUUAU**GCCGAAAGGCUCA**AGUUAAGGAAUGUAGA

Inouye et al. also describes plasmid vector constructs comprising portions of the upstream regulatory sequence of the *cspA* gene linked to a lacZ gene. See col. 9, lines 20-62. In one example is stated that 534 base pairs of the *cspA* upstream regulatory sequence is linked to the lacZ gene, and was capable of up-regulating the expression of the reporter gene construct at 10°C and 15°C, see Table I. See also Examples 4-5.

10. Claims 1, 5-6, 10, and 14-15 are allowable over the prior art.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner
Art Unit 1633

JLE